

lysing the cells, thereby producing a crude extract;

removing insoluble components from the crude extract, thereby producing a refined extract;

dividing the refined extract into first, second, and third extract samples;

separating the first sample into fractions by chromatographic separation with an ion exchange medium;

testing the separated fractions of the first sample to isolate the active fractions of the first sample;

separating the second sample into fractions by chromatographic separation over hydroxyapatite;

testing the separated fractions of the second sample to isolate the active fractions of the second sample;

pooling and concentrating the active fractions of the first and second samples;

separating the third sample into fractions by chromatographic separation over a gel filtration medium;

testing the separated fractions of the third sample to isolate the active fractions of the third sample;

crystallizing the pooled and concentrated active fractions of the first and second sample and the active fractions of the third sample;

analyzing the structure of the crystallized fractions, thereby identifying and isolating new proteasome inhibitors.

22. The method of claim 21, wherein analyzing the structure of the crystallized fractions further comprises collecting data which is compared to known proteasomes, thereby identifying and isolating new proteasome inhibitors.

23. The method of claim 21, wherein analyzing the structure of the crystallized fractions further comprises comparing the crystal structural data from the region of the proteasome pockets S1 of the subunits  $\beta$ 1/PRE2,  $\beta$ 2/PUP2 and  $\beta$ 5/PRE2 to the crystallized fractions, thereby identifying and isolating new proteasome inhibitors.

24. The method of claim 21, wherein analyzing the structure of the crystallized fractions further comprises collecting crystal structural data from the crystallized fractions, and processing that data with a computer-aided modeling program thereby identifying and isolating new proteasome inhibitors.

25. The method of claim 23, wherein the computer-aided modeling program modifies the crystal structural data of a yeast proteasome with amino acid sequences from the human proteasome.

26. The method of claim 21, wherein the three-dimensional structure of the crystallized fractions is complementary to the proteasome pockets S1 of the subunits  $\beta$ 1/PRE2,  $\beta$ 2/PUP2 and  $\beta$ 5/PRE2.